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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/717,051	11/20/2000	Michael S. South	C-3204/2	2191

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EXAMINER	
RAO, DEEPAK R	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 08/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S-M

Office Action Summary	Application No.	Applicant(s)	
	09/717,051	SOUTH ET AL.	
	Examiner	Art Unit	
	Deepak R Rao	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *3-16 and 25-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,17-23,38 and 39* is/are rejected.

7)☒ Claim(s) *40-48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *41801, 62301, 61302* and *123002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-48 are pending in this application.

Election/Restrictions

Applicant's election of Group VI, claims 1, 2, 17-24 (in part) and 38-48 (in part), drawn to compounds (as recited in claim 17) in the reply filed on May 20, 2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Note: *The reference to claim 9 in the description of Group 6 in the previous office action was due to an inadvertent typographical error. As acknowledged by the applicant, this should have been claim ~~9~~ 17.*

Claims 3-16 and 25-37 and the generic portion of claims 1, 2, 17-24 and 38-48 wherein B, A, M and Y^0 are other than those of Group VI are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention(s), there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 20, 2004.

Claim Objections

Claims 40-48 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim can not depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, the claims have not been further treated on the merits.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 38-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inhibiting specific thrombotic condition e.g., treating deep vein thrombosis, does not reasonably provide enablement for inhibiting thrombotic conditions in general. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The use disclosed in the specification is as anticoagulants for the treatment of thrombotic diseases requiring anticoagulant therapy. Test assays to measure inhibition of TF-VIIa, Factor Xa, Thrombin II and Trypsin are provided on pages 209-210 and results for two of the exemplified compounds were provided in Table 1. The procedures merely measure the *in vitro*

inhibition/anticoagulant activity, however, no guidance is provided how this *in vitro* data correlates to *in vivo*. Further, there is no disclosure regarding how this *in vitro* data correlates with 'inhibiting thrombotic conditions' in general. The inhibitory data provided for the exemplified compounds is insufficient such that no reasonable extrapolation could be made by one skilled in the art regarding the activity of the myriad of compounds embraced by the structural formula of the claims. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art (directed to factor Xa inhibitors or anticoagulants) for assuming the same. The area of receptor interactions is highly structure specific and unpredictable. The direction and extent of effects of anticoagulant interactions are not completely predictable. Furthermore, the results of the biological tests appear to be highly structure specific based on the range provided for the measured examples. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art.

The state of the art is not indicative of any anticoagulant agents for inhibiting thrombotic conditions in general. Further there are no known therapeutic or preventative agents for thrombotic conditions generally. The data and evidence provided in the instant disclosure leads the examiner to doubt the objective truth of assertions of inhibiting thrombotic conditions generally. For example, a thrombotic condition such as venous thromboembolism is often clinically silent. As a result, studies evaluating the efficacy of pharmaceutical agents against such condition may not be clinically feasible. Also, the diagnosis of pulmonary embolism with or

without pulmonary infarction is often difficult to establish unless special procedures are used. This clearly establishes the unpredictable nature of thrombotic conditions and neither the disclosure nor the prior art is indicative of any pharmaceutical agents that are effective for generally inhibiting all types of thrombotic conditions.

In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed methods.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 17-24 and 38-39 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 17-24 and 38-39 of copending Application No. 10/215,292 (corresponding Publication No. 2003/0023086). Although the conflicting claims are not identical, they are not patentably distinct from each other because the instantly elected invention substantially overlaps the reference claims. The reference

also teaches and claims compounds that are structurally analogous to the instantly claimed/elected compounds. One of ordinary skill in the art at the time of the invention would have been motivated to select any compounds of the reference genus, including the instantly claimed compound because he would have expected any of the compounds of the reference genus would have the same properties and therefore, the same use as taught for the reference genus as a whole.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Receipt is acknowledged of the Information Disclosure Statement filed on April 18, 2001 (2 sheets); June 23, 2001 (4 sheets); June 13, 2002 (1 sheet); and December 30, 2002 (2 sheets) and copies are enclosed herewith.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Mukund Shah, can be reached on (571) 262-0674. If you are unable to reach Dr. Shah within a 24 hour period, please contact James O. Wilson, Acting-SPE of 1624 at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Deepak Rao
Primary Examiner
Art Unit 1624

August 6, 2004